REMARKS

Claims 19-27 were pending in this application when last examined. Claims 19-22, 24-26 are currently amended. Claim 23 has been canceled and new claim 28 has been added. The amendments further clarify the intended subject matter and address matters of form without adding new matter.

Support for the amendments can be found in the specification and original claims as filed. Support for new claim 28 can be found in original claim 27. No new matter has been added.

CLAIM OBJECTIONS

At page 2, the Office Action objects to the claims because they were misnumbered. The present claims have been renumbered beginning at claim 19, as requested in the Office Action. The Office also notes that the renumbered claims are referred to in the Office Action.

CLAIM REJECTION 35 USC § 112

At page 3, the Office Action rejects claims 21 and 23-27 under 35 U.S.C. § 112, second paragraph as being indefinite. Applicants respectfully traverse the rejection.

The currently amended claims address the issues noted in the Office Action and further clarify the intended subject matter. In particular, the amendments remove the "in particular"

and "such as" features. The "use of" claim 23 has been canceled. The "application of" claim 27 has been canceled and new claim 28 is directed to the intended subject matter of previous claim 27.

In view of the amendments, each of claims 21 and 24-26, as well as new claim 28, satisfies the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CLAIM REJECTION 35 USC § 101

At page 3, the Office Action rejects claim 27 under 35 U.S.C. § 101 because the claim does not set forth any steps involved in the process. Applicants respectfully traverse the rejection.

Amended claim 27 is directed to a method for prognosing tumors that includes the active step of applying the method for *in vitro* diagnosis according to claim 26 to a tumor cell sample. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CLAIM REJECTION 35 USC § 103

At page 4, the Office Action rejects claims 19-22 under 35 U.S.C. § 103(a) as being unpatentable over LEGEAY et al (US 2002/0193885) and CHABRECEK et al. (US 6,436,481).

At page 7, the Office Action rejects claims 23-27 under 35 U.S.C. § 103(a) as being unpatentable over LEGEAY and CHABRECEK in view of ADAIR et al. (US 6,316,215).

Applicants respectfully traverse these rejections.

Claim 19 is directed to a bioactive dish for cell culture. The dish includes a bottom surface and a bilayer coated on the bottom surface, the bilayer comprising an internal primary layer of hydroxypropylmethylcellulose (HPMC) or polyvinyl alcohol (PVA) and an external bioactive layer of carboxypropylmethylcellulose (CMC). LEGEAY and CHABRECEK fail to teach or suggest such a dish.

LEGEAY relates to the construction of a plastic prosthesis that includes a base polymer material coated with a layer of hydrophilic polymer. The Office Action recognizes that LEGEAY is limited to teaching a single layer of either HPMC or PVA and fails to teach a culture dish having a bilayer of HPMC or PVA and a bioactive layer comprising CMC. The Office Action relies on CHABRECEK for teaching the second component (CMC) in a bioactive bilayer.

First, one of ordinary skill in the art would have no reason to modify LEGEAY in such a way. LEGEAY is focused on producing prosthesis material having improved hydrophilicity properties for plastic reconstruction such as mammary and muscular prostheses (see, [0001] and [0002]). The base polymer is modified on its surface by the creation of polar sites and then

coated with a layer of hydrophilic polymer. The idea is to construct material, for example, that reduces the formation of retractile fibrous nodules which lead to a loss of flexibility of the breast and can lead to rupture of the prosthesis membrane (see, [0005]).

One of skill would not consider modifying the polymer coating of LEGEAY to produce a bioactive layer as featured in the present claims. As disclosed in LEGEAY, the hydrophilic nature of their prosthesis "significantly reduces the formation of fibrous nodules over time, probably because of the lower adhesion of the fibroblasts to the envelope surface." (see, [0023]). One of skill would not consider modifying the polymer to produce a bioactive layer that includes a polysaccharide, such as CMC.

Second, LEGEAY teaches that the hydrophilic polymer can be at least one of a list of polymers including HPMC and/or PVA (see, [0045]-[0054]) LEGEAY further states that the hydrophilic polymer can include "a mixture of several of the hydrophilic polymers above, in general a mixture of two or three of the hydrophilic polymers above" (see, paragraph [0055]). Thus, although LEGEAY leaves open the possibility of including more than one polymer, LEGEAY fails to recognize the possibility of including CMC among its list of polymers.

Next, contrary to the position taken in the Office Action, one of ordinary skill would not rely on CHABRECEK for teaching the second component (CMC) in a bioactive bilayer.

CHABRECEK describes coated articles having a primary coating of polymer containing reactive groups and followed with a secondary coating. CHABRECEK does not teach or suggest or direct one toward any particular type of secondary coating, and tries to encompass the universe of "monomeric, oligomeric or macromolecular compounds of synthetic, semisynthetic or biological origin" (See, Abstract and column 5, lines 40-44). Typical secondary coating materials are "peptides, proteins, glycoproteins, carbohydrates, polysaccharides such as collagen, laminin, albumin, extracellular matrix proteins, cell adhesion proteins, growth factors, fibronectin, vitronectin, chondronectin, fibrin, globulins, muscle fibre proteins, vitrogen, genetically engineered peptides and proteins, lectins, hirudin, mucin, chondroitin sulfate, aminodextran, hyaluronic acid, sialic acid, L-fucose, N-acetyl galactosamin and/or derivatives, active fragments and mixtures thereof." (See, column 11, lines 1-13). Lacking from the laundry list of second components in CHABRECEK, however, is any teaching or suggestion toward the use of CMC. Furthermore, CHABRECEK fails to teach or suggest anything regarding the use of CMC in combination with HPMC or PVA.

Another reason why one would not combine the teachings of LEGEAY and CHABRECEK is because the methods of coating the polymer surfaces are different. LEGEAY utilizes a base material "modified on its surface by creation of polar sites." (See,

Abstract). The creation of polar sites increases the surface energy of the base polymer material and "thus encourage the adhesion of the layer of at least one hydrophilic polymer via numerous weak bonds, such as hydrogen bonds, ionic attractions or by Van der Waals forces." (See, [0028], emphasis added).

In CHABRECEK, the support and the polymers are covalently bound. "The present invention relates to coated articles wherein the primary coating comprises a polymer carrying reactive groups. The coating is covalently linked to the surface of the article and exhibits a controlled degree of crosslinking. The invention further relates to the reaction of said primary coatings carrying reactive groups with monomeric, oligomeric or macromolecular compounds ..." (see, column 1, lines 5-12, emphasis added). Also, "Plasma surface treatment in an appropriate vapor ... can therefore be used to place on the surface of any polymeric material reactive chemical groups ... suitable for the subsequent covalent immobilization of various molecules." (See, column 2, lines 57-63, emphasis added).

One of ordinary skill in the art would not consider the covalent bonding reaction conditions of CHABRECEK in combination with the weak bonding (i.e., hydrogen bonds) coating methods of LEGEAY when modifying the coating to include a second CMC component.

Furthermore, it would not have been obvious that surfaces and polymers linked by covalent bonds could also be

linked by hydrogen bonds. One of ordinary skill would not have been able to predict the stability of dishes having HPMC/PVA and CMC linked to the dish surface through hydrogen bonds. Conversely, it would not have been obvious that polymers which form a "bioactive" layer when linked by hydrogen bonds could retain that bioactivity when covalently bonded. The covalent bonds give chemical and physical properties to the polymers that are different from hydrogen bonds.

For all of these reasons, LEGEAY and CHABRECEK fail to teach or suggest, and would not have rendered obvious, a bioactive dish for cell culture having a bilayer coating comprising an internal primary layer made of HPMC or PVA and an external bioactive layer comprising CMC, as featured in claims 19-21. For these same reasons, LEGEAY and CHABRECEK also fail to teach or suggest a method for preparing the bioactive dish as featured in claim 22.

Accordingly, Applicants request reconsideration and withdrawal of the rejection of claims 19-22.

In regard to the rejection of claims 23-27, the Office Action relies on ADAIR for teaching cell culture methods and concludes that it would have been obvious to substitute the culture dishes of the present claims in the bioanalytical methods of claims 23-27. Applicants respectfully disagree with this conclusion.

First, for all of the reasons detailed above, the presently claimed bioactive cell culture dishes would not have been obvious in view of LEGEAY and CHABRECEK; thus, methods that utilize these dishes could also not have been obvious.

Second, one of ordinary skill in the art would not merely substitute one type of dish for another. In particular, one would not substitute a cell culture dish for a bioactive dish having a bilayer coating comprising an internal primary layer made of HPMC or PVA and an external bioactive layer comprising CMC. The presently claimed dishes present an anti-adhesive coating that prevents the adhesion and the spreading of normal adhesive cell, inhibits their proliferation, improves their differentiation and induces apoptosis. The dishes enable the study of mechanisms involved in regulation of proliferation, differentiation and death of normal cells (cellular signals); this application enables the screening of molecules such as anti-aging molecules. The dishes also allow the study of deregulated mechanisms involved in proliferation, the study of the degree of malignancy of cancer cells, measuring their capacity of returning to normal functions and testing the efficiency of therapeutic molecules.

For all of these reasons, LEGEAY, CHABRECEK and ADAIR fail to teach or suggest, and would not have rendered obvious, claims 24-26, as well as new claim 28. Claims 23 and 27 have been

canceled. Accordingly, Applicants request reconsideration and withdrawal of the rejection of claims 24-26.

CONCLUSION

Entry of the above amendments is earnestly solicited. Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX

- a clean copy of the claims